I. Restriction Requirement

With respect to the prior restriction requirement, the Examiner has indicated that claims 3-9 stand withdrawn from consideration. Applicants note that claims 3-9 were cancelled, without prejudice to pursuing the underlying subject matter, at page 5, lines 2-3 of the response filed March 19, 2001. Applicants respectfully request the Examiner to clarify the record.

II. Rejection of Claim 2 under 35 U.S.C. §101/112

Claims 2 and 10-22 are rejected under 35 U.S.C. §101, because the claimed invention is allegedly not supported by a specific, substantial and credible utility or by a well-established utility.

The Examiner asserts that the uses argued by applicants are general and are not specific to the sequences claimed. The Examiner also assert that a nucleic acid molecule may have a utility based on its use as a marker or a probe for a specific disease condition and there is no correlation between specific disease condition and a claimed sequence taught by the instant specification. In addition, the Examiner, starting at page 3, line 15, goes on to argue that a nucleic acid sequence may have a utility based on a protein encoded by the nucleic acid sequence if the protein has a specific and substantial and credible, or a well established utility. However, the Examiner asserts that nowhere does the specification disclose that the claimed sequences actually encode the enzymes in Table A, and that the specification does not disclose open reading frames, start and stop codons of any other information for any sequence would indicate that the claimed nucleic acid sequences encode a protein or a functional peptide.

Applicants respectfully disagree with the Examiner and maintain the position taken in the response filed November 21, 2000. Applicants respectfully request the Examiner to reconsider

the rejection under 35 U.S.C. 101 in view of their previous arguments set forth in the response dated March 19, 2001 and those the follow.

The Utility rejection set forth in the Office Action dated October 17, 2001 based upon two basic premises asserted by Examiner. First, the Examiner asserts that the specification teaches only general uses but does not teach any specific use specific to the sequences claimed. Second, the Examiner asserts that nowhere does the specification disclose that the claimed sequences actually encode the enzymes in Table A, the reading frames of the encoded peptides or proteins, start and stop codons or any other information for any sequence would indicate that the claimed nucleic acid sequences encode a protein or a functional peptide.

The Examiner's assertions are misplaced as the specification clearly asserts that the claimed nucleic acids code for purified maize or soybean tocopherol synthesis pathway enzymes, or fragments thereof. This is addressed, for example, at length in the disclosure starting at page 22, line 14, through page 34, line 21. For at least the foregoing reason, Applicants respectfully submit that the Examiner should withdraw the rejection under 35 U.S.C. 101/112.

In addition to the foregoing, and the utilities discussed at length in their previous response, the specification discloses the instant invention encodes enzymes of the tocopherol synthesis pathway. See the Background of the Invention spanning pages 1-11. Modulation of tocopherol content (including vitamin E) of plant tissues and changes in the levels of the enzymes in the tocopherol pathway can alter both the tocopherol content as well as the compositional quality of the vitamin E family members produced (*e.g.*, page 2, lines 4-8). As the specification discloses that the instant nucleic acids can be used for cosuppression (*e.g.*, page 50, line 5 to page 50, line 13) or antisense suppression (*e.g.*, page 130, line 4 to page 131, line 9), the claimed sequences are useful in altering the levels enzymes of the tocopherol synthesis pathway.

Further to the preceding, Applicants submit that the claimed sequences are useful as probes in the isolation of chromosomes, and for genotyping. In this regard, each sequence is useful for isolating the chromosome on which its corresponding gene is located or determining the geneotype of an individual or plant strain. Applicants submit that the use of the claimed sequences in this manner is analogous to the use of labeled monoclonal antibodies for the isolation of cells in flow sorting in the first instance, and phenotypic/genotypic analysis in the second instance (see for example Leitch et al Nuc. Acids Res. 20(8): 1897-901(1992), abstract attached). Furthermore, both the flow sorting and genotypic analysis ultimately have "real word" value at least in the breading plants, although other utilities can be envisioned.

Applicants again submit that the Examiner "has the initial burden of challenging a presumptively correct assertion of utility in the disclosure." *In re Brana,* 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). The utilities asserted in the specification must be accepted as factually sound unless the Patent Office cites information that undermines the credibility of the assertion. *Id.* The Examiner "must do more than merely question operability - [he] must set forth factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975) (emphasis in original); MPEP § 706.03(a)(1) ("Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided...").

In view of the above, Applicants contend that the claimed nucleic acid molecules are supported by credible, specific, and substantial utilities. Moreover, the Examiner has failed to raise any credible evidence challenging the presently asserted utilities. Consequently, the rejection under 35 U.S.C. §101 is incorrect and should be withdrawn. Applicants further submit

that the assertion that claims 2 and 10-22 under 35 USC 112 first paragraph for allegedly lacking a specific and substantial utility or a well established utility should also be withdrawn in view of the foregoing arguments.

III. Rejection of Claims 1-2 and 10-22 under 35 U.S.C. §112, 1st Paragraph: Written Description

Claims 1-2 and 12-21 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in a manner that reasonably conveys to one of ordinary skill in the art that the inventors had possession of the claimed invention at the time of filing. According to the Examiner, the specification provides insufficient written description to support the invention claimed.

Although the Examiner acknowledges that the Applicants were in possession of the isolated nucleic acid sequences represented by the claimed SEQ ID NOs at the time of invention, the Examiner alleges that the specification provides insufficient written description to support the invention claimed. The Examiner asserts that the instant specification does not teach that any of claimed sequences actually encode a protein or peptide. In addition, the Examiner goes on to assert that homology alone is not sufficient evidence that a protein is encoded by a sequence. The Examiner concludes by asserting that nucleic acid encoding the proteins recited in the claims 1 and 12-22 were not fully described.

Applicants respectfully disagree and maintain the position set forth in the response filed March 19, 2001. Applicants note for the Examiner's attention that the specification clearly asserts that the claimed nucleic acids code for purified maize or soybean tocopherol synthesis pathway enzymes, or fragments thereof. This is addressed at length in the disclosure starting at page 22, line 14, through page 34, line 21, and Table A further describes the sequences. Hence,

the Examiner's assertion that the specification does not teach that any of claimed sequences actually encode a protein or peptide lacks support.

Claims 2 and 10-22 are also rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking written description based upon the assertion that these claims are recited in open claim language and are therefor directed to sequences encompass gene sequences, allelic variants, sequences form other species, etc. The Examiner similarly alleges the specification does not disclose nucleic acid sequences encoding any of the maize or soybean enzymes recited in claim 1, and that the claim 1 is directed to encompass many variants for reach of the recited proteins.

Applicants maintain that they have provided a detailed chemical structure, *i.e.*, the nucleic acid sequence of SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199 and 232. Furthermore, as Table A illustrates, the instant specification provides a functional characterization of each disclosed sequence, by comparingthe claimed sequences to known coding sequences for enzymes of the tocopherol pathway. *See* Example 4, pages 235-236. Persons of ordinary skill in the art routinely characterize function based upon sequence homology.

In view of the foregoing, Applicants assert that the specification meets the burden imposed by *Vas-Cath Inc. v. Mahurkar,* 19 U.S.P.Q.2d 1111, because it "clearly allow[s] persons of ordinary skill in the art to recognize that [Applicants] invented what is claimed." Moreover, by presenting SEQ ID NOs: 1, 100, 147, 153, 158, 161, 180, 184, 199 and 232, Applicants have provided a detailed chemical structure of the claimed nucleic acids and thereby meet the burden set forth in *Fiers v. Revel* 984 F.2d 1164, 25 U.S.P.Q.2d 1601 (Fed. Cir. 1993), *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991), *Fiddles v. Baird*, 30

U.S.P.Q.2d 1481, 1483 (Fed. Cir. 1993) and *Regents of the University of California v. Eli Lilly & Co.*119 F.3d 1159, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997).

In view of the foregoing arguments and the amendments, Applicants respectfully request that the rejections under 35 U.S.C. §112, 1st paragraph be withdrawn.

IV. Rejection of Claim 2 under 35 U.S.C. §112, 1st Paragraph: Enablement

Claims 2 and 12-21 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention.

The Examiner alleges that the sequences disclosed by Applicants do not set forth reading frame that would allow the skilled artisan to make a protein or peptide. The Examiner goes on to assert that eukaryotic genes often comprise multiple reading frames for any given sequence and that the instant specification does not disclose any amino acid sequences that can be used to "line up" encoding polynucleotides. In addition, the Examiner alleges the specification does not teach the peptides required to align the sequences, the specific enzyme assays required or data base and parameters employed to generate the homology data in Table A. Based on the foregoing the Examiner asserts that it would require undue experimentation to make and use the invention of claims 2 and 12-21.

Applicants respectfully disagree and maintain that the position set forth in the response filed March 19, 2001. In addition, Applicants submit that the Examiner's position is based upon several incorrect assumptions. First, the Examiner's assertion that the specification does not teach the specific enzyme assays is completely misplaced. Assays for each of the enzymes corresponding to a claimed nucleic acid sequence are art recognized, and a patent need not teach, and preferably omits what is well knowing the art. *Hybritech v. Monoclonal Antibodies*, Inc.,

802 F.2d 1367, 1384, 231 U.S.P.Q. 81, 94 (Fed Cir. 1986). Moreover, the Examiner's assertion that the data base and parameters employed to generate the homology data in Table A were not disclosed by Applicants is incorrect. Example 4 on pages 235-236 the specification sets forth that the data base employed was Genebank and default parameters were used.

Moreover, Applicants respectfully disagree with the Examiner's assertion that Applicants do not set forth reading frame that would allow the skilled artisan to make a protein or peptide, and that the multiple reading frames for any given rise to undue experimentation. Applicants submit that there are only three possible reading frames for a nucleic acid strand. Applicants submit that performing routine and well-known steps cannot create undue experimentation even if it is laborious. *In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976).

Applicants reiterate that the Examiner has not met the evidentiary burden required to impose an enablement rejection. A specification that discloses how to use the claimed invention "must be taken as in compliance with the enabling requirement of the first paragraph of §112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995), quoting *In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphasis in original). The Examiner has provided no objective evidence supporting the rejection. See *In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510,1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement). Moreover, the Examiner's explanation as to why the specification fails to enable such uses is based upon unsupported assumptions. In view of the foregoing, Applicants submit

that the rejections of claims 2 and 12-21 is incorrect and respectfully request the Examiner to reconsider and withdraw the rejection of record[1].

V. Rejection under 35 U.S.C. §112 second paragraph

Claims 1-21 are rejected under 35 U.S.C. 112 second paragraph as allegedly being indefinite for the recitation of "said nucleic acid." Applicants respectfully disagree with the Examiner as that the recitation was intended to refer to the isolated nucleic acids as clearly indicated in the preamble of the claim. In order to advance prosecution, however, Applicants have amended the claims to recite "said isolated nucleic acid," thereby rendering the rejection moot. In view of the foregoing, Applicants respectfully request the withdrawal and reconsideration of the rejection under § 112 second paragraph.

VI. Rejection under 35 U.S.C. §102

Claims 1 and 10 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Eichholtz (WO 92/06201) and Claim 1 is rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Brown *et al.* (US 5,859,347).

To facilitate prosecution, Applicants have amended claims 1 and 10 to delete reference to the enzyme EPSP. Applicants submit that this renders the rejection moot, and respectfully request the Examiner to withdraw the rejection.

[1] Applicants note that independent claims 1 and 10 have not been included in the instant rejection.

The Examiner is invited to contact the undersigned at (202) 942-5000 with respect to any unresolved issues remaining in this application.

Respectfully submitted,

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MARKED UP VERSION OF THE CLAIMS PURSUANT TO 37 C.F.R. 121

1. (Twice Amended) A substantially purified nucleic acid molecule that encodes a maize or soybean tocopherol synthesis pathway enzyme or fragment thereof, wherein said maize or soybean tocopherol synthesis pathway enzyme is selected from the group consisting of:

(a) deoxyarabiono-heptulosonate-P-synthase or fragment thereof;

(b) putative deoxyarabiono-heptulosonate-P-synthase or fragment thereof;

(c) dehydroquinate synthase or fragment thereof;

(d) dehydroquinate dehydratase or fragment thereof;

(e) putative dehydroquinate dehydratase or fragment thereof;

[(f) shikimate dehydrogenase or fragment thereof;]

(f)[(g)] shikimate kinase or fragment thereof;

[(h) enolpyruvylshikimate-P-synthase or fragment thereof;]

(g) [(i)] chorismate synthase or fragment thereof;

(h) [(j)] chorismate mutase or fragment thereof;

(i) [(k)] tyrosine transaminase or fragment thereof;

(j) [(l)] putative tyrosine transaminase or fragment thereof;

(k) [(m)] transaminase A or fragment thereof;

(l) [(n)] putative transaminase A or fragment thereof;

(m) [(o)] homogentisic acid dioxygenase or fragment thereof; and

(n) [(p)] geranylgeranylpyrophosphate synthase or fragment thereof.

2. (Twice Amended) The substantially purified nucleic acid molecule according to claim 1, wherein said nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 100, SEQ ID NO: 147, SEQ ID NO: 153, [SEQ ID

NO: 158,] SEQ ID NO: 161, SEQ ID NO: 180, [SEQ ID NO: 184,] SEQ ID NO: 199, and SEQ ID NO: 232.

10. (Once Amended) An isolated nucleic acid molecule comprising a sequence that hybridizes under conditions of 2.0 X sodium chloride/sodium citrate (SSC) at about 65°C to a nucleic acid molecule having a sequence selected from the group consisting of SEQ ID NOs: 1, 100, 147, 153, [158,] 161, 180, [184,] 199, and 232 and complements thereof.

11. (Once Amended) The isolated nucleic acid molecule, according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 100, SEQ ID NO: 147, SEQ ID NO: 153, [SEQ ID NO: 158,] SEQ ID NO: 161, SEQ ID NO: 180, [SEQ ID NO: 184,] SEQ ID NO: 199, and SEQ ID NO: 232.

12. (Once Amended) The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule [encodes a maize deoxyarabiono-heptulosonate-P-synthase and said nucleic acid molecule] comprises a nucleic acid sequence of SEQ ID NO:1.

13. (Once Amended) The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule [encodes a soybean deoxyarabiono-heptulosonate-P-synthase and said nucleic acid molecule] comprises a nucleic acid sequence of SEQ ID NO:100.

14. (Once Amended) The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule [encodes a soybean putative deoxyarabiono-heptulosonate-P-synthase and said nucleic acid molecule] comprises a nucleic acid sequence of SEQ ID NO:147.

15. (Once Amended) The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule [encodes a maize dehydroquinate synthase and said nucleic acid molecule] comprises a nucleic acid sequence of SEQ ID NO:153.

16. (Once Amended) [The] An isolated nucleic acid molecule [according to claim 10, wherein said isolated nucleic acid molecule encodes a maize putative dehydroquinate dehydratase and said nucleic acid molecule comprises] comprising a nucleic acid sequence of SEQ ID NO:158 or complements thereof.

17. (Once Amended) The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule [encodes a maize shikimate kinase and said nucleic acid molecule] comprises a nucleic acid sequence of SEQ ID NO:161.

18. (Once Amended) The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule [encodes a soybean shikimate kinase and said nucleic acid molecule] comprises a nucleic acid sequence of SEQ ID NO:180.

20. (Once Amended) The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule [encodes a maize chorismate synthase and said nucleic acid molecule] comprises a nucleic acid sequence of SEQ ID NO:199.

21. (Once Amended) The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule [encodes a soybean chorismate synthase and said nucleic acid molecule] comprises a nucleic acid sequence of SEQ ID NO:232.